

ANNUAL REPORT
OF
THE HOWE LABORATORY
OF
OPHTHALMOLOGY
HARVARD MEDICAL SCHOOL
AT THE
MASSACHUSETTS EYE AND EAR
INFIRMARY

1972

243 CHARLES STREET

BOSTON, MASSACHUSETTS 02114

HOWE LABORATORY OF OPHTHALMOLOGY
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This Annual Report is being sent to you in the hope of maintaining your interest in, and possible support of, eye research in the Howe Laboratory. On the continued goodwill and assistance from many of you depends the Laboratory's ability to pursue those humanitarian and scientific goals which have characterized its 45 year history.

A handwritten signature in dark ink, reading "David G. Cogan". The signature is written in a cursive, flowing style. The first name "David" is written in a more compact, blocky cursive, while "G. Cogan" is more elongated and fluid.

David G. Cogan, M.D.
Director

The Howe Laboratory has had an unsettling year, one in which continuation of basic research in a clinical setting has been at stake. The departure of several senior investigators left a void that has been difficult to fill. The Infirmary's vigorous building program has entailed major uncertainties in allocations of space, selection of personnel, coordination with other research activities, and methods of funding. At the same time the development of ophthalmic facilities in the Medical School area has raised the question of relocating the Laboratory within the Harvard system. And the imminent retirement of the present Director has limited long range planning.

These disruptions were anticipated but our plans for abetting them have been only partially successful. We are, nevertheless, holding the line with faith that prudent decisions in the forthcoming year will reestablish the stability of the Laboratory and reaffirm its commitment to fundamental research. In the meantime we can report significant progress in various endeavors and productive participation in a variety of clinical and academic activities. We have again had the privilege of generous support of many individuals and agencies. This Report is prepared primarily in appreciation of these benefactions.

GLAUCOMA AND INTRAOCULAR FLUID DYNAMICS

Loss of vision from glaucoma is due to damage of the fibers of the optic nerve by excessive intraocular pressure. Nearly always excessive pressure in the eye is caused by some obstruction to drainage of the aqueous humor that is continuously secreted into the eye. Research has been concentrated upon four main factors that affect the vision and the pressure in glaucoma: (1) damage to the optic nerve, (2) secretion of aqueous humor into the eye, (3) the outflow system by which the aqueous humor escapes from the eye, and (4) involvement of the lens with tendency to formation of cataract. Each of these factors has been studied in the Howe Laboratory.

Secretion of aqueous humor into the eye has been studied mainly with an aim of finding and improving ways to reduce the rate of this secretion and thereby reduce the intraocular pressure. In

glaucoma the rate is seldom found to be excessive, but it has been proven of great practical value in treatment of glaucoma to reduce the rate of aqueous formation below normal to compensate for obstruction to drainage. Aqueous formation may be reduced surgically or medically. Currently the principal procedure under clinical investigation for reducing aqueous secretion surgically is cyclocryo-treatment, or low temperature freezing of the ciliary body that produces the fluid. This has been evaluated clinically by Dr. Bellows and several associates, to determine how to do this most effectively and safely.

Variables such as temperature and site of localized freezing of the eye in relation to effectiveness of pressure reduction and frequency of complications have been further evaluated this year but the final answers will take more time to determine.

An important medical means that is currently utilized for reducing aqueous secretion is treatment with drugs that inhibit the enzyme carbonic anhydrase. These must be taken by mouth or given intravenously. These drugs have been used in the treatment of glaucoma for nearly two decades, since their effectiveness was discovered practically simultaneously in the Howe Laboratory and at the Wilmer Institute. They have been administered to a large proportion of patients whose glaucoma has been difficult to control, and in a great many cases they have made it possible to control the pressure and to avoid surgery. However, there have been many systemic side effects that have made it difficult or impossible for some patients to use these drugs even though they seriously need them for control of their glaucoma. Dr. Grant has made an extensive survey for the Drug Committee of the American Academy of Ophthalmology and Otolaryngology of the information that has accumulated on side-effects of these drugs, and on possible means to reduce or prevent some of their undesirable actions. The aim of this study and of continuing work on the problem is to find out how to counteract the side effects so that patients who need these drugs to avoid surgery or loss of vision may be able to take them more safely and pleasantly.

The outflow system by which the aqueous humor escapes from the eye has this year again been a focus of both experimental and clinical glaucoma research in the Howe Laboratory, as it has for

many years. More than two decades ago Dr. Grant initiated a series of studies on human and animal eyes in the laboratory based on perfusion of the eyes with physiologic fluids at measured rates and pressures to simulate the secretion and flow of aqueous humor in the eye as it occurs in life. Comparisons that have been made with measurements obtained by clinical tonography in patients have indicated that perfusion provides a reasonable simulation of conditions in life. This aqueous perfusion procedure in enucleated eyes has been used in many studies by Dr. Grant and his associates, most recently by Drs. Bruce Ellingsen, Johnstone and Van Buskirk, particularly in studying the functional characteristics of the aqueous outflow channels, the abnormalities that are characteristic of glaucoma, and the mode of action of many factors that influence the facility of aqueous outflow. This series of studies by means of quantitative aqueous perfusion in enucleated eyes, and parallel clinical studies of aqueous outflow by means of tonography originated in the Howe Laboratory, have had fundamental influences on study and progress in treatment for glaucoma in many parts of the world. Developments in microsurgery of Schlemm's canal in recent years have been most intimately related to these experimental studies. In 1970, Dr. Ellingsen provided us with new evidences suggesting that there may be varying degrees of apposition of the inner wall of Schlemm's canal to the outer wall of the canal, and that this is apparently favored by increase in intraocular pressure and is particularly notable in eyes with open-angle glaucoma. It has seemed likely that varying degrees of collapse of the canal might be a significant factor determining the area available for drainage of aqueous humor from anterior chamber of the eye to the aqueous and episcleral blood-containing veins. Dr. Ellingsen also provided evidence suggesting that some of the effects of making an opening from within the eye of Schlemm's canal by trabeculotomy, and some of the effects of exteriorizing Schlemm's canal by Professor Krasnov's sinusotomy, may be explained by the fact that when either wall of Schlemm's canal is removed it prevents the pressing of one wall against the other and eliminates the interference with drainage attributable to collapse of the canal.

This year, Dr. Johnstone has proceeded further with studies of the aqueous outflow system of the human eye, investigating not

only the functional factors with aqueous perfusion and dissection techniques, but he has in addition examined the morphologic features of the aqueous outflow system by means of light microscopy and scanning electron microscopy looking for physical changes of tissue and cellular configurations to relate to variations in facility of aqueous outflow. He has made some remarkable observations.

Dr. Johnstone has found that the configuration of the trabecular meshwork and endothelial walls of Schlemm's canal undergo striking changes in relation to the pressure in the eye and the amount of fluid flowing through these tissues. With increasing pressure and increasing aqueous outflow the endothelium of the inner wall of Schlemm's canal is found to develop progressively larger and more numerous vacuoles, the subendothelial zone expands, the inner wall of the canal approaches the outer wall, and at elevated pressures occludes portions of the lumen of the canal. This type of response has been demonstrated in human eyes after enucleation and in the eyes of a living monkey. When pressure relationships were reversed, there appeared to be an arrangement analogous to a one-way valve preventing blood from passing from Schlemm's canal back into the anterior chamber of the eye, yet allowing blood to escape from the eye with flow of aqueous in the normal direction.

The flow characteristics, the one-way valve action, and the associated reversible changes in configuration of this portion of the aqueous outflow system all appear to be analogous to what is known of the behavior of the arachnoid villae in the central nervous system where the cerebrospinal fluid, which is analogous to the aqueous humor of the eye, passes through a highly specialized structure to the blood stream. The arachnoid villae have been known for some time to change configuration in response to variations in pressure and flow, and to act as a one-way valve to prevent blood from flowing back into the cerebrospinal fluid. The trabecular wall of Schlemm's canal appears to have similar actions with respect to aqueous humor and blood circulation in the eye.

The changes in configuration in response to rate and direction of aqueous flow that Dr. Johnstone has demonstrated in the aqueous outflow system of the eye has provided a new basis for studying and understanding what goes wrong in glaucoma and how drugs and surgery of various types may help in treatment of glaucoma.

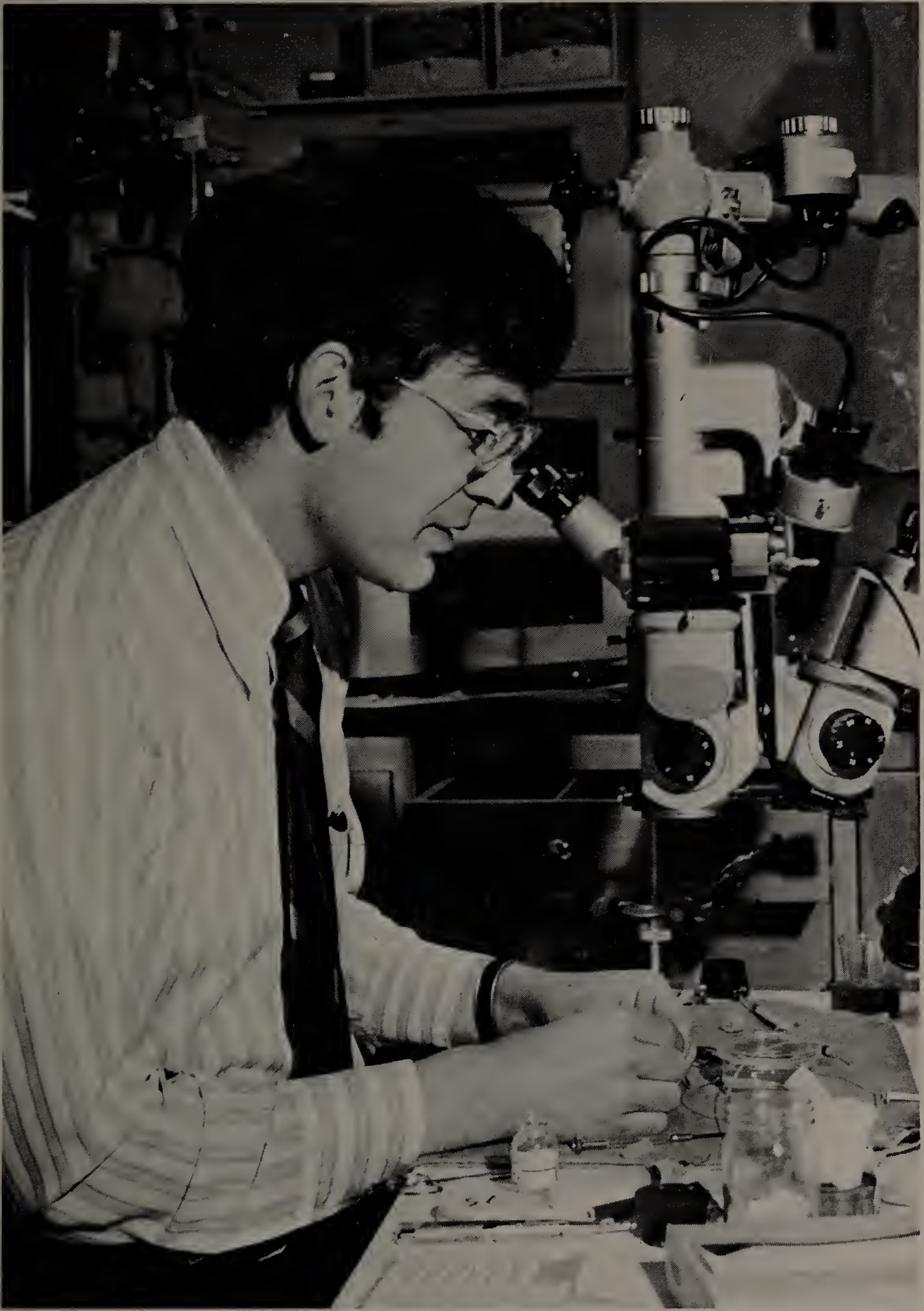
A second series of studies carried out this year by Dr. Johnstone has concerned the microsurgical procedures on Schlemm's canal that have been employed in treatment of glaucoma in numerous ophthalmologic centers in various parts of the world in the last few years. In particular, Dr. Johnstone has examined the effects of a procedure known as trabeculotomy ab externo, which was a logical outgrowth of earlier studies in the Howe Laboratory that demonstrated that obstruction to aqueous outflow in glaucoma could be eliminated by making an opening from the anterior chamber to Schlemm's canal. A high proportion of clinical successes has been reported from the use of this surgical procedure, but post-operative examination of patients has raised questions whether the procedure actually has worked in the manner in which it was intended. In particular this question has arisen in a group of patients in whom Drs. Richard Simmons and Johnstone have performed trabeculotomy ab externo.

In the original experiments by Dr. Grant the opening from anterior chamber to Schlemm's canal had been made internally by means of a cystotome with an internal cutting edge, whereas in the clinical procedure of trabeculotomy ab externo a wire is inserted into Schlemm's canal from an external incision and is caused to slide circumferentially in the canal like a ram-rod before it is twisted centrally to tear open the trabecular meshwork into the anterior chamber. Dr. Johnstone has repeated the internal trabeculotomy experiments and confirmed that internal cystotome trabeculotomy markedly reduced resistance to aqueous outflow, as previously shown by Dr. Grant and by Dr. Ellingsen, but he found that the ab externo probe trabeculotomy seldom accomplished this. Initially it seemed that the flaps of tissue produced by rupture of the trabecular meshwork might be returning to their original position and again obstructing outflow. To eliminate this factor a diathermy probe previously devised by Dr. Ellingsen was inserted circumferentially in Schlemm's canal in the same manner as the commonly employed wire probe, but the diathermy probe was insulated on all sides except the side toward trabecular meshwork. When a high frequency electric diathermy current was passed through this special probe, it produced a gaping opening from Schlemm's canal to the anterior chamber. Despite this elimination

of complicating flaps of the trabecular meshwork, the facility of aqueous outflow was seldom found to be improved. Finally it was found that simply inserting a wire probe circumferentially in Schlemm's canal and removing it without either rupturing or cauterizing the trabecular meshwork tended to cause an increase in resistance to aqueous outflow, which is the opposite of the therapeutic aim of the whole surgical procedure. By microscopic examination, utilizing dissecting microscope, scanning electron microscopy, and light microscopy of 1 micron sections, Dr. Johnstone found evidence that this simple insertion of the probe in Schlemm's canal caused drastic flattening of structures of the outer wall of the canal, and it appeared likely that this could account for the interference with aqueous outflow which resulted from insertion of the probe. Dr. Johnstone then compared the local tissue effects of the original internal cystotome trabeculotomy procedure which previously had been found so effectively to reduce resistance to aqueous outflow, and he found that this procedure not only provided a direct opening from anterior chamber to Schlemm's canal but also appeared to tear or disrupt some of the structures of the outer wall of the canal, including some of the openings of the aqueous veins from the canal. These comparisons made it seem likely that the internal trabeculotomy procedure facilitates drainage of aqueous through the peripheral aqueous outflow channels, but that the ab externo procedure most likely depends upon producing an artificial fistula through the sclera to the surface of the eye.

While all these details of morphology and change in configuration of the outflow system in relation to normal function and in relation to glaucoma and surgical procedures for glaucoma may seem complicated and difficult to unravel, we think they are important in coming to a better understanding of glaucoma and its treatment.

Dr. Van Buskirk has been investigating other aspects of the aqueous outflow system, utilizing quantitative aqueous perfusion and microscopic examination of human and monkey eyes, examining in particular the mechanism by which blood cells leave the anterior chamber of the eye and pass through the aqueous outflow system, but are normally prevented from re-entering the eye through this same system. Also Dr. Van Buskirk has been seeking



DR. VAN BUSKIRK manipulates tissue, with the aid of a dissecting microscope, in his study of the aqueous outflow system.

additional information relating physical configuration of the outflow system and the facility of aqueous outflow. He has devised a means for simulating the physical action that miotic eyedrops are

believed to exert on the tissues of the outflow system when they are effective in treatment of glaucoma. It has long been conceived that miotic eyedrops cause contraction of a portion of the ciliary muscle that simultaneously exerts traction on tissues of the aqueous outflow system around Schlemm's canal and affects the tension in the zonules to the lens and the focusing of the crystalline lens. Dr. Van Buskirk has simulated the contraction of the ciliary muscle by applying a graded traction to it through the zonules of the lens. He has found that the facility of aqueous outflow determined by quantitative aqueous perfusion in enucleated eyes responds to this traction by a graded and reversible increase. This is presumed to be analogous to the increase in facility of outflow which is measured by tonography in the eyes of patients under the influence of miotic eyedrops. Now that Dr. Van Buskirk has established the functional effect of this procedure, his aim is to establish what the morphologic or configurational modifications may be in the tissues of trabecular meshwork and Schlemm's canal to explain the change in the ease with which the aqueous humor flows through these tissues under the influence of miotic treatment.

As more is learned of the relationships of tissue morphology and the hydrodynamics of the aqueous outflow system, the better we should be able to define and correct what is abnormal in glaucoma.

Dr. Grant in his dual role of supervising glaucoma research in the Howe Laboratory and directing the Infirmary's Glaucoma Consultation Service has had opportunities to study aspects of glaucoma which may be infrequently encountered in individual practices, and in doing this has called freely upon the experience and advice of Drs. Paul A. Chandler and Simmons and many other members of the Visiting and Resident Staffs of the Infirmary.

In the recent past, this type of cooperative study has proved particularly instructive and productive in arriving at better understanding and much improved treatment of malignant glaucoma. This year Dr. Grant with the cooperation of other interested ophthalmologists has carried out a study of the late glaucomas that have been seen in increasing number in recent years in patients who had interstitial keratitis in childhood. A study of 70 cases of old interstitial keratitis in adult patients, of whom 60 had glaucoma, established that the glaucoma fell into two main categories, one

of which was primarily an open-angle glaucoma associated with signs of old inflammatory processes in the angles, and this form of glaucoma proved to be peculiarly unresponsive to medical treatment, but fortunately to respond to filtering surgery without unusual complications. In the other main category of late onset glaucoma, after childhood interstitial keratitis, the anterior portions of the eyes were found to be congenitally smaller than normal, and they appeared in later life to become overcrowded as a result of the lifelong continuing growth of the lens within the eye. In these patients angle-closure glaucoma was typical, and this as a rule has proved curable or has been greatly benefited by iridectomy. What has been learned from this study should be helpful in future cases in diagnosis and in choice of treatment.

Dr. Grant has also continued a study of a syndrome of unilateral shallowing of the anterior chamber and angle-closure glaucoma following occlusion of the central retinal vein, now having recognized this condition in 8 cases since he was first alerted to the possibility by an observation by Dr. Alfred W. Scott, in 1960. The significant practical importance of recognizing this syndrome is that this represents a rare exception in which one may expect the angle-closure glaucoma to resolve spontaneously within a few weeks while kept under control with medical treatment, and may avoid the necessity of operation which is almost mandatory in more common types of angle-closure glaucoma.

Among the long term glaucoma research projects on which Dr. Grant has continued work this year have been the documentation of optic nerve changes by stereophotography with Dr. Donaldson (see p. 19), the study of pathogenesis and treatment of glaucoma in aniridia with Dr. Walton, the evaluation of cycloplegic tonography in diagnosis of glaucoma, and constant expansion of the cross-reference file of information on all aspects of glaucoma from all parts of the world, a resource that is constantly called upon for help in answering clinical and experimental research questions.

W. Morton Grant, M.D.

CATARACTS AND BIOCHEMISTRY

Under Dr. Kinoshita's direction, the main theme of biochemical research in the Howe Laboratory for the past several years has

been cataracts. This has been notably successful, especially in elucidating the processes involved in the development of sugar cataracts such as are encountered occasionally in diabetes and in galactosemia. The cataract studies are now being continued under the joint leadership of Drs. Chylack and Fukui.

Infantile cataracts and hexokinase

A form of cataract is known to occur in certain infants with a low blood sugar, an entity known as neonatal hypoglycemia. This clinical observation has led Dr. Chylack to study and characterize the enzyme hexokinase which is the pacemaker of glycolysis in the lens. Two forms of soluble hexokinase have now been recovered from the lens. One form, classical Type II, is heat labile at 37.5°C and is rapidly deactivated in the intact lens or in the homogenate used to prepare hexokinase for study but is completely stabilized by physiological levels of glucose. A second form of hexokinase has been found to be insoluble or bound hexokinase. The respec-



DR. CHYLACK adjusts an incubation tube in which he cultures the lens while varying the environmental milieu.

tive roles of these two forms will now be studied in vitro and in animals.

Glutathione and ascorbic acid

Their high concentration in the normal lens and their depletion as cataracts develop have given glutathione and ascorbic acid a prime position in metabolic studies of the lens. They are thought to be critically involved in the oxidation-reduction processes that are necessary for the proper functioning of such avascular structures as the lens. Drs. Fukui and Epstein, with the helpful participation of Dr. Hong-Ming Cheng, have studied the ascorbic acid and glutathione relationships in the rat lens. Ascorbic acid reacts with oxygen non-enzymatically to produce dehydro-ascorbic acid and hydrogen peroxide. The hydrogen peroxide then appears to penetrate the lens and oxidize the lens glutathione through the enzyme glutathione peroxidase. The oxidized glutathione can in turn be reduced in the lens by glutathione reductase. This process accounts



DR. FUKUI makes precise measurements of ascorbic acid to be added to his lens culture medium.

for one very important link in the chain of energy reactions that maintain the normal transparency of the lens.

The viability of the lens is reflected in its ability to concentrate potassium. A standard method for testing this function is the uptake of labelled rubidium (^{86}Rb). Rat lenses incubated with 20 mg % ascorbic acid without glucose for one hour demonstrate a 35% decrease in ^{86}Rb uptake. Incubation in the presence of $2 \times 10^{-5}\text{M}$ cupric sulfate further doubles the ascorbic acid effect. But incubation with glucose or catalase in the medium prevents both of these ascorbic acid effects.

The uptake of ^{86}Rb decreases with the addition of either hydrogen peroxide (1mM.) or dehydroascorbic acid (20 mg %) to the medium in the absence of glucose. The complete reversal of the ascorbic acid effect in the presence of catalase indicates that the observed decreases in ^{86}Rb uptake is due mainly, if not totally, to the hydrogen peroxide generated from the oxidation of ascorbic acid in the medium.

NEURO-OPHTHALMOLOGY

The investigative aspects of neuro-ophthalmology are directed chiefly toward unravelling the complex circuitry of the human brain. Much of the information comes from clinical examinations where tell-tale signs and symptoms point to specific sites of lesions. Other information must come from animal experimentation where tracts of nerve fibers may be traced to remote terminals. The clinical and experimental approaches are often far apart. One of the missions of the Howe Laboratory has been to connect the two by maintaining intimate contact with patients while exploring experimental approaches in animals. Sometimes this is successful, sometimes not.

Optic neuritis and multiple sclerosis

Because of its frequency and serious consequences, multiple sclerosis has been a patient-oriented concern of the Laboratory for many years. A very practical problem to which Dr. Wray has recently directed her research efforts has been an attempt to determine which patients with optic neuritis will develop multiple sclerosis and which will not. It is known that a significant number,

estimated between 15-40%, will develop other manifestations of the systemic disease but the individual patient with an acute attack of optic neuritis cannot at present be given an accurate prognosis as to vision, possibility of recurrences, or prospects for long term health.

Neuro-immunological studies have been carried out by Dr. Wray on patients with optic neuritis and on animals with experimentally induced demyelinating disease with the aim of developing a reliable diagnostic test for demyelination. Antigen types have been determined in white cells from 30 patients with optic neuritis and compared with the antigen types of 56 control persons and persons with overt multiple sclerosis. The latter observations, performed in conjunction with Dr. Barry Arnason and Dr. Thomas Fuller at the Massachusetts General Hospital, indicated a significantly high incidence of certain antigen types (known to tissue typists as HL-A₃, HL-7, and HL-8) in patients with multiple sclerosis but no uniform association of these antigen types with optic neuritis as compared with normal controls. The prognostic value of these observations and the application of tissue typing in patients with optic neuritis can be assessed only on completion of a long term study when it will be possible to determine what proportion of these patients with optic neuritis have developed multiple sclerosis.

Paralysis and apparent paralysis of down-gaze

This unusual symptom was investigated by Dr. Cogan on the basis of clinical cases in which it was a prominent feature and on the basis of one histopathologic study. The findings indicated that paralysis of down-gaze could occur either as a reverse Parinaud's syndrome with lesions below the Aqueduct of Sylvius in the anterior mid-brain or with diffuse brain stem disease in association with choreo-athetosis or with Parkinsinoid syndromes. The reverse Parinaud's type is frequently a manifestation of vascular disease and is a true paralysis whereas the second type is associated with retention of the vestibulogenic movements and may result from hypertonia of the antagonist muscles rather than a true paralysis.

Anatomic studies

Having finished his neuro-ophthalmic fellowship, Dr. Bienfang

has this past year embarked on an experimental study aimed at localizing the centers for conjugate horizontal gaze in the brain stem. Using a new technique under the provident guidance of Dr. Walle Nauta (Massachusetts Institute of Technology), Dr. Bienfang is applying a radioactive amino acid to selective portions of the central nervous system of animals and then tracing the movement of labelled protein along the nerve fibers.

Neurophysiologic studies

A noteworthy example of laboratory application to clinical problems in neuro-ophthalmology is Dr. Fricker's extensive investigations into quantitation of the visual and ocular motor responses. With a background in electronic engineering prior to his medical training, Dr. Fricker has been able to establish a laboratory for: (1) recording the retinal response to a flash of light by means of a unique phase delay system; (2) measurement of the conduction time from the eye to the brain to within fractions of a millisecond; and (3) record the velocity, acceleration, and frequency of eye movements for a variety of stimuli. With the engineer's commitment to precise numbers and a clinician's aim to evaluate signs, Dr. Fricker is amassing a thesaurus of controlled observations that have important relevance to problems in diagnosis and to the evaluation of therapy. This past year Dr. Deppermann joined this section of the Laboratory. With a background in neurology, Dr. Deppermann's studies have related to the ocular movement disturbances in parkinsonism and the specific effects of L-dopa.

With Mr. Sanders, Dr. Fricker has been engaged in model studies in which electroretinographic signals and background noise were studied under controlled and specified conditions. In actual recordings it is often not clear what the reliability of the measurements may be, and what accuracy may be obtained for time and amplitude parameters. By statistical evaluation of the results of these model studies, some approximate numerical solutions have been obtained relating to the probability of detection of a given type of signal, and what signal-to-noise ratio is needed in order to achieve a certain specified accuracy in amplitude and timing measurements.

Miscellaneous

The curious and often chaotic movements of the eyes included under the term opsoclonus were analyzed by Dr. Bienfang in a group of children. It appears that, unlike the condition in adults, opsoclonus in children is frequently associated with mental retardation and therefore carries with it a poorer prognosis.

HISTOLOGY AND PATHOLOGY

Dr. Kuwabara's departure left a big gap in the Laboratory's functions in experimental pathology and electron microscopy. Fortunately, however, we have been able to secure the appointment of Dr. Pihlaja and, most recently, of Dr. Yasuna Hamai, both of whom bring unusual talents to this important area of the Laboratory's researches. Dr. Pihlaja comes from the Department of Anatomy at the Harvard Medical School with an impressive back-



DR. PIHLAJA at the console of the scanning electron microscope.

ground in electron microscopy. Dr. Hamai hails from Japan, where his interests have related to histochemistry and ultrastructure of the eye.

While becoming familiar with the "eye field", Dr. Pihlaja has undertaken several exploratory studies. One, done with Dr. A. L. Norton, was the experimental production of serous retinal detachment by lysis of Bruch's membrane with observations on the ultrastructural changes in the choriocapillaris, pigment epithelium, and photoreceptors. A second direction of study has been the determination of electron microscopic changes in cataract formation. This has been correlated with the biochemical investigations of Drs. Fukui and Chylack. Still other collaborative studies in the formative period are the role of "tight junctions" in the corneal epithelium as regulators of corneal permeability, a study initiated with Dr. Don DiBona (Massachusetts General Hospital,) and an investigation into the role of conjunctival cells in the repair of corneal wounds undertaken with Dr. David Miller. Electron microscopy has become an essential part of any project dealing with tissue.

Prior to his return to Japan, Dr. Imaizumi completed a study of that curious process by which nuclei are extruded from the lens cells during the maturation of lens fibers. These cells are akin to red blood cells, but unlike all other cells in the body in losing their nuclei during growth and thereby losing their capacity for further programming of their metabolism. Yet these cells survive for long periods. Dr. Imaizumi found by electron microscopy that holes appear in the nuclear membrane through which the DNA leaks out. This process is distinctly different from the simple extrusion which occurs in the case of red blood cells.

The continuing interest of Dr. Cogan in the pathology of vascular diseases in the eye has led to the uncovering of a new cause for occlusion of the retinal vein. Based on the observations in one case, it appears that calcific emboli lodging in the central artery within the optic nerve behind the lamina cribrosa may so compromise the circulation as to produce the clinical picture of primary venous occlusion in the eye. The characteristic clinico-pathologic features of embolic occlusion of the retinal arteries have been analyzed on the basis of the abundant documentation at the Infirmary and the Howe Laboratory and are being prepared for inclusion in

a forthcoming text on ophthalmic manifestations of systemic vascular disease.

Dr. Cogan has also had the opportunity of making an in-depth study of the histopathology of retinitis pigmentosa based chiefly on specimens that were obtained through the courtesy of the National Institutes of Health.

Tumors of the optic nerve present important clinical and pathologic problems in differential diagnosis. The considerable number of cases listed in the files of the Infirmary and the Howe Laboratory were analyzed this past year by Dr. Cogan and comprise the substance of a chapter in a forthcoming Handbook of Neurology. A further study of these gliomas together with those from the Massachusetts General Hospital, were made by Dr. Adam Borit during his three months' study in the Howe Laboratory and constitutes one of the largest series analyzed histopathologically.

ULTRASONOGRAPHY

A perennial limitation of diagnostic ophthalmology has been detection of abnormalities that cannot be visualized ophthalmoscopically when the cornea or lens is opaque. Similar difficulties are encountered in the diagnosis of mass lesions in the orbit that produce protrusion of the eye and give only indirect evidence of their nature or localization. But in recent years ultrasonography has emerged as a most useful technique for detecting and outlining such lesions and Dr. Dallow has embarked on a long-term exploration of its applicability to clinical problems. Earlier studies, beginning in 1960, were made with successive steps of technical improvements, by Drs. Grant, Andrew Dahl and Robert Gorn.

Ultrasonography consists of the propagation of high frequency sound waves through tissue and their differential reflection from objects in the beam path. The ultrasonic energy is partially reflected from anatomic interfaces, creating echoes which are then displayed on an oscilloscope screen much as in sonar or radar systems. Integration of the scanned beams permits a cross-sectional visualization of the eye and orbit that yields a two-dimensional picture of structures that cannot be seen by any other method. In the technical vernacular, this is called B (for "brightness") scan ultra-

sonography in contrast to the former technique designated A (for "amplitude") scan ultrasonography that merely gave a one dimensional echo.

With the latest apparatus, Dr. Dallow has confirmed the feasi-



DR. DALLOW applying ultrasonography to the eye of a patient with suspected intraocular disease.

bility of ultrasonography for the detection and localization of otherwise occult detachments of the retina, tumors, foreign bodies, hemorrhage, and inflammatory infiltrations. The technique has proved so valuable that we are now making arrangements to move the applied aspects out of the research area into the service area where we anticipate it will take a place along with radiology and fluoroangiography as an essential diagnostic procedure. At the same time we anticipate continuation of laboratory research into the development of improved electronic hardware that will simplify the technique and make it less costly.

STEREOPHOTOGRAPHIC DOCUMENTATION

Unique photographic methods have been developed by Dr. Donaldson over the years for documentation of many clinical conditions. Much of the effort this past year has been directed toward recording changes in the optic nerve head resulting from glaucoma. In cooperation with Drs. Grant, Chandler, and other ophthalmologists, serial stereo-photographs have been made of the nerve heads in several hundred patients with glaucoma. Because Dr. Donaldson's stereoscopic camera takes two photographs simultaneously, the stereoscopic effect is constant and thereby allows for accurate comparisons between various photographs of the same individual. A further step in the analysis is subjecting these pictures to the process of stereophotogrammetry which is now being undertaken with an outside firm specializing in this type of work. The process is similar to that of stereoscopic aerial photography which involves analysis of stereoscopic pairs in a complicated machine that produces drawings of the contours or sections of the optic nerve with a high degree of accuracy. From this data the exact volume of the nerve head can be determined and minute changes in the amount of cupping can be ascertained which would otherwise be undetectable.

Photographs of slow growing iris tumors taken over a period of 15 years have been similarly subjected to volumetric analysis as well as exact contours of the cornea and depth measurements of the anterior chamber.

With Dr. Chandler's encouragement and financial help, a second stereoscopic camera for fundus photography has now been completed and is in the testing stages prior to being stationed in the Glaucoma Consultation Service. A valuable improvement in the design of this second camera is a lighting system that permits photography of the nerve head with minimal dilatation of the pupil. The stereoscopic viewing system for focussing prior to the photography has also been modified to allow for greater accuracy and ease of focussing.

During his fellowship, Dr. Waltman reviewed all the tumors of the iris and ciliary body that are in Dr. Donaldson's photographic collection and correlated them with what histopathologic material

was available. A similar study was made of pseudoexfoliation of the lens. Selected examples of both conditions will be included in Dr. Donaldson's forthcoming Atlas.

TEACHING

It is now more than 30 years since a postgraduate course in the basic sciences in ophthalmology was organized at Harvard. This course, initially staffed almost entirely by the Howe Laboratory, is believed to have been the first of its kind in the country. It served as a model for similar courses elsewhere, including that large course organized by Dr. Lancaster, to accommodate the many veterans of World War II who could not be taken into the Harvard course.

These courses have supplied a need that neither the undergraduate medical school nor the hospital residencies provided at that time. But recently the attitude of the medical schools have changed in the direction toward incorporating specialty training into the undergraduate curriculum. In view of this, Dr. Alfred Scott and Dr. Cogan offered an elective course as a pilot project covering much of the material previously given in the postgraduate course. Having completed its third year, this course has been well received by the students* (about ten each year) and has been stimulating to the teachers. It is our prediction that similar courses, established in schools that have faculties willing to give the time to it, will be an effective means of attracting superior students into ophthalmology. Certainly, the future effectiveness of ophthalmic care depends on the quality of the medical students who now elect ophthalmology as a career.

Various members of the Howe Laboratory staff continued teaching activities as noted in previous reports. Dr. Donaldson and Dr. Wray conduct neuro-ophthalmology sessions, Dr. Cogan, pathology sessions, and Dr. Grant, glaucoma sessions in Harvard's Basic Sci-

* Excerpts of a letter received this past year from one of the students reflects a type of appreciation that makes the teaching effort worthwhile: "Before graduation, and leaving town to begin an internship this summer, I wanted to extend a special note of thanks . . . rarely is a medical student so fortunate . . . I can say with certainty that the course was instrumental in my decision to pursue a career in ophthalmology"

ence Course in Ophthalmology, while Drs. Wray and Cogan repeated their intensive week-long course in neuro-ophthalmology.

AWARDS AND HONORS

While some years have passed since Dr. Carl Kupfer was a member of the Howe Laboratory and the director of its training program, we nevertheless feel a prideful glow to read that he received the Department of Health, Education and Welfare's Special Citation for "outstanding performance in the development of the National Eye Institute". This is the first HEW Citation since 1966.

During 1972 Dr. Cogan served as Visiting Professor at Northwestern University (February), at Vanderbilt University (April), and at Tulane (May) and was appointed the American Editor for Graefes Archiv für Ophthalmologie. Dr. Wray was an invited faculty member of the first course in neuro-ophthalmology at the Hospital for Nervous Diseases, Queen Square, London and was Visiting Scientist to the Academic Unit at the Institute of Neurology, London.

ORGANIZATION

The Howe Laboratory is approaching that climax which occurs to some degree whenever there is a change of Directorship but which has been unusually disruptive in the present instance by simultaneous organizational changes in the Department of Ophthalmology and the Infirmary. The fundamental question which is currently being weighed is how can academic research serve best the cause of science and the welfare of mankind in the framework of the Howe Laboratory.

Despite these disruptions we have continued to probe new ventures of an organizational nature in keeping with current needs and opportunities. An especially noteworthy arrangement has been worked out whereby clinicians with a research interest rotate their clinical obligation at the Peter Bent Brigham Hospital with research activities in the Howe Laboratory on a one week-two week schedule. Thus Drs. Chylack, Bienfang, and Bellows "cover" the ophthalmic services at the Brigham while conducting their researches

at the Laboratory. This arrangement, a modification of the former Howe Laboratory Consultation Service, enables the continuation of basic research in the face of clinical demands. It seems to be working well.

APPRECIATION

The many persons and agencies who have chosen to support eye research through the Howe Laboratory deserve more thanks than can be transmitted in a simple Report. Each benefactor has been a real participant in whatever has been accomplished and deserves a full measure of credit. While it is true that the complexities of research and dependence on expensive equipment have necessitated increasing support from Federal agencies, especially the National Institutes of Health, the support of private agencies and individuals has provided a freedom in probing new avenues that cannot be readily supplied by governmental sources. We are indebted to the Massachusetts Lions Eye Research Fund, Inc., to the Genradco Trust, to Research to Prevent Blindness, Inc., to the other philanthropic trusts and to many individuals recorded in the appended list.

We would especially like to cite Mr. J. M. Ulmer whose death occurred toward the end of the year just passed. Mr. Ulmer was a Cleveland lawyer who had devoted much of his time and energy to furtherance of ophthalmic research during the last three decades of his 86 years. A frequent visitor to the Laboratory he had first hand contact with the laboratory personnel and the support of their research. Believing that the future depended on encouraging new investigators, he made an annual award to that young person in the Howe Laboratory who had made a most significant contribution through unusual industry and creativity. We shall miss Mr. Ulmer's many faceted support, his visits, and frequent telephone calls.

EPILOGUE

While contemplating the successes and failures in organizational activities of this past year, and of other years, we came across the

following quotation (Wall Street Journal, November 9, 1972) taken from another's Annual Report. At the risk of being overly glib about such a serious matter, we cite it as being humorously germane: "Our company, as you know, has had good years and bad years. As president, it gives me a great deal of pleasure to report that 1972 has been one of them."

DAVID G. COGAN, M.D.

Director

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Ultrastructure of retina and retinal disease

Studies of iris ultrastructure

Differentiation of chick retina

Studies on diabetic retinopathy

Correlation analysis of eye motions, ERG and VER

PUBLICATIONS

CHADER, G. J.

with Reif-Lehrer, L.: Hormonal effects on the neural retina: Corticoid uptake, specific binding and structural requirements for the induction of glutamine synthetase. *Biochim. Biophys. Acta* 264:186-196, 1972.

CHYLACK, L. T., JR.

with Kinoshita, J. H.: The interaction of the lens and vitreous. Part I. The high glucose cataract in a lens-vitreous preparation. *Exp. Eye Res.* 14:58-64, July 1972.

COGAN, D. G.

with Kuwabara, T.: Growth and regenerative potential of Descemet's membrane. *Trans. Ophthal. Soc. U.K.* 91:875-894, 1971.

with Kuwabara, T.: Tumors of the ciliary body. *Int. Ophthalmol. Clin.* 11(#3):27-56, Fall 1971.

Heredity of congenital ocular motor apraxia. *Trans. Amer. Acad. Ophthalmol. Otol.* 76:60-63, January 1972. Also in *Contemporary Ophthalmology*, St. Louis, Mosby, 1972. pp 52-56.

Radiant Energy. Section IV of Vol. 2 of *Modern Ophthalmology*, 2nd Ed. Edited by A. Sorsby. London, Butterworths, 1972. pp 685-691.

Benign vacuolated melanomas of the ciliary body. Chapter in *Contemporary Ophthalmology*. Edited by J. G. Bellows. Baltimore, Williams and Wilkins, 1972. pp 377-381.

DONALDSON, D. D.

A new instrument for keratography. *Arch. Ophthalmol.* 88:425-428, October 1972.

FRICKER, S. J.

Use of synchronous detector for ERG and VER measurements in children. Proceedings of VIII ISCERG Symposium, September 7-12, 1970, Pisa, Italy. Edited by A. Wirth. Published Pisa (Italy), 1972.

GRANT, W. M.

with Ellingsen, B. A.: Trabeculotomy and sinusotomy in enucleated human eyes. *Invest. Ophthalmol.* 11:21-28, January 1972.

Laboratory Research Symposium: Microsurgery of the outflow channels. *Trans. Amer. Acad. Ophthalmol. Otol.* 76:398-404, March-April 1972. Also in *Contemporary Ophthalmology*. St. Louis, Mosby, 1972. pp 142-148.

Drug intoxications and chemical injuries. Chapter in *Modern Ophthalmology*. Edited by A. Sorsby, London, Butterworths, 1972. pp 661-683.

JEDZINIAK, J. A.

with Kinoshita, J. H., Yates, E. M., Hocker, L. O. and Benedek, G. B.: Calcium-induced aggregation of bovine lens alpha crystallins. *Invest. Ophthalmol.* 11:905-915, November 1972.

WRAY, S. H.

The treatment of optic neuritis. *Sight-Sav. Rev.* 42:5-13, Spring 1972.

LECTURES

APPEN, R. E.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
Some traumatic neuro-ophthalmologic syndromes, October 17, 1972.
Cranial trauma and ocular motility disturbances, November 8, 1972.

BELLOWS, A. R.

New England Ophthalmological Society:
Tumor and angiogenesis factor in aqueous of eyes containing intraocular neoplasm, March 15, 1972.
Xeroderma pigmentosum with ocular tumors. Report of a family. December 20, 1972.
Chairman, Yale Symposium, December 20, 1972.
Complication Conference: Management of flat anterior chambers in the early post-operative period. House Officer Lecture, Massachusetts Eye and Ear Infirmary, August 1972.
Cyclocryotherapy in advanced uncontrolled glaucoma. Ophthalmic Staff, Massachusetts Eye and Ear Infirmary, January 1972.

BIENFANG, D. C.

Opsoclonus. New England Ophthalmological Society, January 19, 1972.
Department of Ophthalmology, University of Florida, in Gainesville, Florida, February 10, 1972:
Opsoclonus.
Pleomorphic adenoma of the nasopharynx.
Unusual cause of cavernous sinus syndrome. Neuro-ophthalmic Pathology Symposium, in Chicago, Illinois, February 26, 1972.
Supranuclear disorders of gaze. Department of Ophthalmology, Albany Medical Center, April 4, 1972.
Postgraduate Course in Neuro-ophthalmology, Harvard Medical School, April 24-30, 1972:
Strabismus for the neurologist.
Case presentations.
Ischemic optic neuropathy. Division of Vascular Surgery, Peter Bent Brigham Hospital, July 22, 1972.
Neuro-ophthalmology. House Officer Lecture, Massachusetts Eye and Ear Infirmary, August 8, 1972.
Postgraduate Course in Ophthalmology, Harvard Medical School:
Neuro-ophthalmology of brain stem, September 11, 1972.
Disorders of gaze, September 11, 1972.
Disorders of the orbit, November 16-17, 1972.
The cavernous sinus syndrome. Department of Neurology, Peter Bent Brigham Hospital, September 23, 1972.
Some neuro-ophthalmic emergencies. Maine Regional Medical Seminars, Bates College, in Lewiston, Maine, November 22, 1972.

Introduction to neuro-ophthalmology. Series of monthly lectures to the Third Year Class, Harvard Medical School, January-December 1972.

CHYLACK, L. T., JR.

Basic ophthalmology for practitioners in family medicine. Family Health Center, Harvard Medical School, January 1972.

Chronic progressive ophthalmoplegia externa. Neurology Grand Rounds, Peter Bent Brigham Hospital, February 1972.

External diseases of the eye. Elective in Ophthalmology. Fourth Year Class, Harvard Medical School, March 1972.

Northeastern University:

Traumatic lesions in ophthalmology, March 20, 1972.

Physiology of injury and repair of the eye, March 27, 1972.

Cataracts and uveitis. Fourth Year Class, Harvard Medical School, March 23, June 22, September 21, and October 19, 1972.

Sugar metabolism in the lens. Flower and Fifth Avenue Hospital, in New York, New York, April 10, 1972.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:

Lens metabolism and cataract formation, April 12, 1972.

Lens physiology, September 26, 1972.

Thermolability of rat lens hexokinase. Association for Research in Vision and Ophthalmology, in Sarasota, Florida, April 26, 1972.

Human lens hexokinase. Symposium on Aging and the Lens, Medical University of South Carolina, in Charleston, South Carolina, September 20, 1972.

Postgraduate Course in Ophthalmology, Harvard Medical School: Metabolic diseases affecting the eye, November 21, 1972.

Uveitis — basic mechanisms, December 8, 1972.

COGAN, D. G.

Clinical pathology. Lecture series. Elective Course, Harvard Medical School, January-February 1972.

Hallucinations. New England Ophthalmological Society, January 19, 1972.

Blackouts of vascular origin. Nashville Academy of Ophthalmology, in Nashville, Tennessee, March 13, 1972.

Postgraduate Course in Neuro-ophthalmology. Lecture series. Harvard Medical School, April 24-29, 1972.

Common neuro-ophthalmological problems. Seventh O'Brien Visiting Professor, Tulane University and New Orleans Academy of Ophthalmology, in New Orleans, Louisiana, May 7-9, 1972.

Neuro-ophthalmic pitfalls. American Association of Neurological Surgeons, in Boston, April 18, 1972.

Retinal emboli. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 26, 1972.

Discussion: The lesions producing paralysis of downward but not upward gaze, by L. Jacobs, P. J. Anderson and M. B. Bender. American Neurological Association, in Chicago, Illinois, June 12, 1972.

- Discussion: Neuro-ophthalmology. Division of Neurology. St. Vincent Hospital, in Worcester, August 22, 1972.
- Clinical and pathological aspects of cataract. Lens and Aging Symposium, Medical University of South Carolina, in Charleston, South Carolina, September 19, 1972.
- Ophthalmic pathology. Series of lectures. Postgraduate Course in Ophthalmology, Harvard Medical School, September 25–October 19, 1972.
- Diabetic retinopathy. Symposium on Diabetes Mellitus, New York University Postgraduate Medical School, in New York, New York, September 28, 1972.
- Systemic diseases of the eye. Introduction to the Clinic, Third Year Class, Harvard Medical School, October 6, 1972.
- Testimonial to A. R. Levine, Jr. Estelle Doheney Eye Foundation, in San Francisco, California, October 23, 1972.
- Paralysis of downward gaze. Neuro-ophthalmology Conference, Tufts University School of Medicine, Division of Ophthalmology, December 27, 1972.

DALLOW, R. L.

- B-Scan ultrasonography. New England Ophthalmological Society, May 26, 1972.
- Diagnostic ultrasonography of the eye and orbit. Lancaster Courses in Ophthalmology, in Waterville, Maine, August 18, 1972.
- Diagnostic ultrasound. House Officer Lecture, Massachusetts Eye and Ear Infirmary, August 24, 1972.
- Infrared photography of the ocular fundus. Twenty-fifth Anniversary Congress of the Retina Service, Massachusetts Eye and Ear Infirmary, September 18, 1972.
- Current ophthalmological research on blinding disease. Board of Education and Services for the Blind, State of Connecticut, in Wethersfield, Connecticut, November 3, 1972.
- Postgraduate Court in Ophthalmology, Harvard Medical School: Physics and technology of ultrasound, November 30, 1972.
- Ocular diagnosis by ultrasound, December 4, 1972.
- Orbital diagnosis, artifacts and development aspects of ultrasound, December 14, 1972.
- Diagnostic ultrasound. Retina Service Fellows, Massachusetts Eye and Ear Infirmary, December 6, 1972.
- Ophthalmic ultrasonography. Massachusetts Lions Eye Research Fund, Inc., December 13, 1972.
- Diagnostic ultrasonography in ophthalmology and obstetrics-gynecology. IEEE Meeting on Sonics and Ultrasonics, Massachusetts Institute of Technology, in Cambridge, December 20, 1972.

DONALDSON, D. D.

- Diseases of the cornea. Society for Contemporary Ophthalmology, in Hollywood, Florida, February 28–March 4, 1972.
- Ocular signs of systemic disease, especially diabetes. Scientific Session of Massachusetts Ophthalmological Society, April 12, 1972.

- Special techniques in stereophotography. Symposium on Stereophotography as a Clinical and Experimental Tool, Association for Research in Vision and Ophthalmology, in Sarasota, Florida, April 24-28, 1972.
- Ocular injuries. Course in Industrial Ophthalmology, Harvard School of Public Health, May 24, 1972.
- Systemic disease involving cornea. Postgraduate Course in Corneal Disease, Harvard Medical School, June 8, 1972.
- Common problems involving the eye. Meeting of Family Physicians, in Bedford, New Hampshire, June 9, 1972.
- Infections of the eye. New Hampshire Academy of Family Practice, in Manchester, New Hampshire, June 14, 1972.
- Blowout fractures. Recovery Room Lecture, Operating Room Nurses, Massachusetts Eye and Ear Infirmary, June 21, 1972.
- Iris atrophy, systemic diseases involving the cornea. Michigan Ophthalmological Society, in Bellaire, Michigan, July 21-22, 1972.
- External eye disease. Lancaster Courses in Ophthalmology, in Waterville, Maine, August 21-23, 1972.
- External diseases and ocular photography. University of Pennsylvania Postgraduate Course, in Philadelphia, Pennsylvania, October 10-14, 1972.
- Recent developments in recording lens opacities. Microwave Conference, in Pacific Grove, California, November 13-15, 1972.
- Collagen diseases. Arthritis Seminar, Massachusetts General Hospital, December 18, 1972.
- Postgraduate Course in Ophthalmology, Harvard Medical School: Neuro-ophthalmology, August 29-November 27, 1972.
- Enucleation complications and blowout fracture repair complications, October 19, 1972.
- Diseases of the anterior segment, November 4-December 13, 1972.
- House Officer Lectures, Massachusetts Eye and Ear Infirmary:
- Corneal disease, January 11-12, 1972.
 - Systemic disease, April 5, 1972.
 - Photography of the eye, April 6, 1972.
 - Enucleation complications and blowout repair complications, October 19, 1972.
 - Diagnosis and management of orbital trauma, November 2, 1972.

FRICKER, S. J.

- Optic nerve lesions. Fourth Year Class, Harvard Medical School, January 8, July 8 and October 5, 1972.
- Patterns of horizontal nystagmus. New England Ophthalmological Society, January 19, 1972.
- Strabismus and amblyopia. Visiting Nurses Association, in Boston, January 26, 1972.
- ERGs and VERs. Department of Ophthalmology, Albany Medical College, in Albany, New York, February 3, 1972.

Electrical measurements in ophthalmology. Eastern New York State Ophthalmological Society, in Albany, New York, February 3, 1972.

Clinical patterns of nystagmus. Association for Research in Vision and Ophthalmology, in Sarasota, Florida, April 27, 1972.

ERGs, VERs and eye motion. Northeastern University Extension Course, in Boston, May 8, 1972.

Numerical measurements of horizontal eye motion. Smith-Kettlewell Institute of Visual Sciences, in San Francisco, California, May 11, 1972.

Electrophysiological measurements and the injured eye. Alumni Association of the Massachusetts Eye and Ear Infirmary, May 25, 1972.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
 Physiology of eye muscles, May 17, 1972.
 Strabismus, July 6, 1972.
 Complications of strabismus surgery, September 28, 1972.

Electrophysiology. Postgraduate Course in Ophthalmology, Harvard Medical School, September 11 and 18, 1972.

Lazy eye. Medical Call, WCVB-TV, in Boston, October 16, 1972.

GRANT, W. M.

Symposium on Glaucoma. Louisiana State University Medical Center, in New Orleans, Louisiana, January 21 and 22, 1972:
 Angle closure glaucoma: Medical therapy.
 Open-angle glaucoma: Tonometry and tonography.
 New drugs in the treatment of glaucoma.
 Surgery and experimental studies on Schlemm's canal.
 Malignant glaucoma diagnosis and treatment.
 Neovascular glaucoma.

House Officer Lectures, Massachusetts Eye and Ear Infirmary:
 Review of filtering operations and cyclocryotherapy in glaucoma, May 2, 1972.
 Ocular toxicology of common systemic medications, May 16, 1972.
 Glaucoma and uveitis, July 11, 1972.
 Ocular pharmacology, September 12, 1972.

Recent glaucoma research. National Eye Institute, in Bethesda, Maryland, May 26, 1972.

Oregon Ophthalmological Alumni Association, in Portland, Oregon, September 7 and 8, 1972:
 Aniridia.
 Systemic medications and glaucoma.
 Interstitial keratitis with glaucoma.
 Aqueous dynamics and surgery of Schlemm's canal.

American Academy of Ophthalmology and Otolaryngology and Association for Research in Vision and Ophthalmology, in Dallas, Texas, September 24, 1972:
 Antiglaucoma drugs: Problems with carbonic anhydrase inhibitors.

Symposium on drugs.
 Postgraduate Course in Ophthalmology, Harvard Medical School:
 Toxicology, September 20 and November 27, 1972.
 Tonometry and tonography, November 6, 1972.
 Glaucoma in infants, December 7, 1972.
 Drugs and the eye. Introduction to the Clinic, Harvard Medical School, October 11, 1972.
 Miscellaneous glaucoma problems. Eye Conference Lecture, Massachusetts Eye and Ear Infirmary, November 22, 1972.
 Discussion: Infection and inflammation. The source of new vessels in a case of rubeosis iridis. V. L. Jocson. New England Ophthalmological Society, December 20, 1972.

JOHNSTONE, M. A.

Glaucoma. Postgraduate Course in Ophthalmic Nursing, Massachusetts Eye and Ear Infirmary, February 1, 1972.

SNYDER, C.

The introduction of ether into ophthalmic surgery. House Officer Lecture, Massachusetts Eye and Ear Infirmary, February 9, 1972.
 The history of ophthalmology through the eyes of patients. Postgraduate Course in Ophthalmology, Harvard Medical School, September 13 and 18, 1972.
 Genius must pay its price or, the doctor and his doxie. Benjamin Waterhouse Medical Historical Society, in Boston, October 16, 1972.

WRAY, S. H.

New England Ophthalmological Society:
 See-saw nystagmus, January 19, 1972.
 Ocular myopathy in children, January 19, 1972.
 Discussor: Vertical ocular motor dysmetria, December 20, 1972.
 Germinoma of the pineal. Neuro-ophthalmic Pathology Meeting, in Chicago, Illinois, February 25-26, 1972.
 Nystagmus and posterior fossa lesions. Neuro-ophthalmic Rounds, Boston University, March 3, 1972.
 The eye and multiple sclerosis. Multiple Sclerosis Society, in Franklin, Massachusetts, March 16, 1972.
 Neuro-ophthalmology. Postgraduate Course in Neurology, Harvard Medical School, at Massachusetts General Hospital, March 21, 1972.
 with Cogan, D. G., Joint Director: Postgraduate Course in Neuro-ophthalmology, Harvard Medical School, April 24-29, 1972.
 Ocular myopathy. First Neuro-ophthalmology Course, National Hospital for Nervous Diseases, Queen Square, in London, England, May 1-5, 1972.
 Visiting Neurologist to the Institute of Neurology, in London, England, May 8-12, 1972.
 Oculomotor nerve function. House Officer Lecture, Department of Neurology, Massachusetts General Hospital, June 2, 1972.

Dural shunts. Neurosurgical Grand Rounds, Massachusetts General Hospital, June 15, 1972.

Massachusetts Eye and Ear Infirmary Staff Rounds:

- Monocular amaurosis fugax, July 26, 1972.
- Binocular amaurosis fugax, August 2, 1972.
- Painful isolated peripheral nerve lesions, August 9, 1972.
- Painful combined peripheral nerve lesions, August 23, 1972.
- The pupil, August 30, 1972.

Visiting Consultant Neurologist to the Adult Neurology Service, Massachusetts General Hospital, Daily Rounds, September 1-30, 1972.

Management of lesions in the region of the sella turcica. Postgraduate Course in Neuroradiology, Harvard Medical School, October 16-20, 1972.

Postgraduate Course in Ophthalmology, Harvard Medical School:

- Ocular myopathy and myasthenia, November 3, 1972.
- Nystagmus, November 10, 1972.

FORM OF BEQUEST

The Howe Laboratory of Ophthalmology is an independent department of the Harvard Medical School and is jointly supported by a restricted endowment of Harvard University and by the Massachusetts Eye and Ear Infirmary.

For the information of those who may wish to contribute to this Laboratory, a form of bequest is here set forth:

I GIVE AND BEQUEATH TO THE HOWE LABORATORY OF
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TO BE APPLIED TO THE USES OF SAID LABORATORY.

Such bequests are managed by the Treasurer's Office of Harvard University and are tax deductible. The income is accredited to the Laboratory.

